cells against each other with mortar and pestle. However, this procedure left many whole cells in the aqueous medium, which then could not be separated from cell nuclei. This fraction was therefore essentially useless and had to be discarded, posing a serious difficulty when Claude wanted to characterize the distribution of a given enzyme by stating the amount in later, usable fractions relative to the amount in the whole cell. Two biochemists at Wisconsin, Conrad Elvehjem and Van Potter, developed a coaxial homogenizer in which finely cut or minced tissue was placed in a tube with some buffered salt solution and a closely-fitting pestle rotated either by hand or with a motor while being worked up and down in the tube. Although this may seem like a gentle procedure, it is not. It breaks the membrane through the shearing force resulting from the faster moving material near the pestle rubbing against the slower moving material near the wall of the tube. As a result, the Elvehjem-Potter homogenizer was quite effective at breaking cell membranes, but it also broke some internal membranes (Potter & Elvehjem, 1936). By the estimate of de Duve (1971), it damaged 15% of lysosomes and peroxisomes and 10% of mitochondria. It is interesting to consider how de Duve could reach such a judgment. As we will see, he made a fundamental assumption – that a given enzyme originated in a single organelle. Thus, he inferred that the fraction with the greatest concentration was the locus of the enzyme in living cells, and that any of the enzyme found in other fractions represented contamination. This was plausible insofar as the amount of an enzyme found in one fraction generally greatly exceeded that in any other. In this instance, it was the determinateness of the results that supported the judgment of what was artifact and what was evidence of an underlying phenomenon.

Several factors affect the degree of disintegration of cells achieved with the Potter-Elvehjem homogenizer, including the clearance between tube and pestle, the speed of rotation, and the number of times the pestle is moved up and down. This led to a striking number of variations in the basic design of the homogenizer, some of which are illustrated in Figure 4.2. Campbell and Epstein (1966, p. 19) commented, "it is probably true that almost every worker has his own individual preference." A variety of other means of breaking cell membranes were explored in the 1940s and 1950s, including colloid mills (employed by Mirsky to isolate chromosomes, as in Mirsky & Ris, 1951), ultrasonic or sonic vibrations, and osmotic shock. Most investigators, though, adopted the Elvehjem-Potter homogenizer or variants on it. This was largely because it provided a successful compromise between the destructiveness of the Waring blender and the insufficient disruption of membranes from simple rubbing. It produced impressive, interpretable results (clear differentiation of